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**BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

Paper No. 17

Application Number: 09/744,574
Filing Date: April 05, 2001
Appellant(s): ELGER ET AL.

Csaba Henter
Anthony J. Zelano
For Appellant

**EXAMINER'S ANSWER**

This is in response to the appeal brief filed 04/21/2003

*(1) Real Party in Interest*

.A statement identifying the real party in interest is contained in the brief.

*(2) Related Appeals and Interferences*

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

*(3) Status of Claims*

The statement of the status of the claims contained in the brief is correct.

*(4) Status of Amendments After Final*

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

*(5) Summary of Invention*

The summary of invention contained in the brief is correct.

*(6) Issues*

The appellant's statement of the issues in the brief is incomplete. Note that there is also an outstanding provisional double patenting rejection in the instant application.

*(7) Grouping of Claims*

The appellant's grouping of claims is correct.

*(8) Claims Appealed*

The copy of the appealed claims contained in the Appendix to the brief is correct.

*(9) Prior Art of Record*

5,314,694 Gale et al. 05-1994

WO 96/05216 Siemann et al. 02-1996

*(10) Grounds of Rejection*

The following ground(s) of rejection are applicable to the appealed claims:

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 8-17 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 23 and 24 of copending Application No. 09/755,429. Although the conflicting claims are not identical, they are not patentably distinct from each other because the employment of the estrogen sulfamate in

hormone replacement therapy method of claims 8-15 of the instant application is encompassed by the Formula I compounds used in hormone therapy method of claims 23-24 of copending Application No. 09/755,429.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 8-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Siemann et al. in view of Gale et al. (USPN 5,314694).

Siemann et al. (WO 96/05216) teaches novel estra-1,3,5,(10)-triene amidosulphamates. When R1, R2, R4, R5, R6 and R8 are each H and R7 and R9 are OH, the formula I structure is that of estriol-3-sulphamate within the instant claims, see particularly page 8. Siemann et al. (WO 96/05216) further teaches employing these compounds in compositions and methods for hormone replacement therapy, see abstract. Siemann et al. (WO 96/05216) also teaches the dosage to be 10 microgram of estradiol, ethinyl-estradiol and estriol per animal per day, see table I.

Siemann et al. (WO 96/05216) does not teach the use of gestagens in its method of hormone replacement therapy; neither does it teach the continued administration of the gestagen.

Gale et al. (USPN 5,314694) teaches the employment of an estrogen along with norprogestrone, in a device useful for continuous transdermal administration, in a method of hormone replacement therapy in women, see claims 11, 13 and 19, col.13-14.

It would have been obvious to one of ordinary skill in the art to employ the estrogen sulfamates in Siemann et al. (WO 96/05216) in combination with gestagens in methods of hormone replacement therapy. It would have also been obvious to administer the gestagen in a continuous manner.

One of ordinary skill in the art would have been motivated to employ a gestagen along with any of the compounds of Siemann et al. (WO 96/05216) in a method hormone replacement therapy because both gestagens and estrogen sulfamates are known to be useful in hormone replacement therapy methods. Combining two agents which are known to be useful in hormone replacement therapy methods individually into a single composition useful for the very same purpose is *prima facie* obvious. See *In re Kerkhoven*, 205 USPQ 1069. At least additive therapeutic effects would be reasonably expected. Please note that the method of making a composition by merely mixing or combining ingredients is considered *prima facie* obvious.

***(11) Response to Argument***

***Appellant has not rebutted the provisional obviousness double patenting rejection in his appeal brief and has thus acquiesced to the rejection.***

Although a provisional obviousness-type double patenting rejection was made and maintained during the prosecution, appellant has not rebutted the rejection in his brief, thus it is believed that the appellant has acquiesced to the double patenting rejection.

***The requirement for a prima facie case of obviousness is whether the Skilled Artisan in possession of the teachings in the prior art would have arrived at the instant invention, and not whether the Skilled Artisan should arrive at the invention.***

Appellant argues that the question to be asked in the obviousness rejection is not whether one could achieve intermittent administration, but whether the prior art teaches that those of skill in the art should use intermittent administration. Note that the prima facie case of obviousness is based on whether one of ordinary skill in the art *would* have arrived at the instant invention, given the teachings of the prior art references.

**Intermittent administration instead of daily administration of known pharmaceutical compositions is an optimization of regimen, within the purview of the Skilled Artisan.**

Appellant argues that intermittent administration is not an optimization of regimen when the prior art only teaches daily administration. Note that the employment of estradiol sulfamate and gestagens for Hormone Replacement Therapy (hereinafter HRT) is known in the art. Variations and/or optimizations of the dosage regimen of compounds well known to be useful in HRT together sequentially or simultaneously are considered within the skill of the artisan, absent evidence of the contrary. No such evidence is seen. Note that attorney's arguments as to unexpected results do not take the place of clear and convincing data.

Appellant then argues that estrogen is known to be quickly eliminated from the body. Applicant refers to prior art references to support this proposition. Applicant refers specifically

to figures 9 and 10 on page 86 of one of the Elger publications, Expert. Opin. Invest. These prior art references have been reviewed by the Examiner and the following points can be deduced:

- The concentration of estradiol sulphamate is close to zero, 24 hours after administration.
- The subjects are rats and the daily dosage is 10 microgram per animal per day (or 70 microgram per animal per week).

Claim 1 recites the administration of a dosage of 20-300 microgram per day in intervals of 2 or 3 days. Assuming *arguendo* 23.3 microgram is administered to a woman in 2 day intervals, the weekly dosage of estradiol sulphamate will be 70 microgram per week. Therefore the prior art dosages fall within the claimed dosages. The review of the prior art as well as the applicant's statement that the release of the noted hormones from the sulfamate prodrug proceeded more slowly in humans than in rats. Indicates that rat is not a good model for human given the difference in estradiol sulphamate release profile in the two subjects. Therefore the showing of the prior art is not clear and convincing.

Relying on a **simulated** figure, applicant argues that after the 4$^{th}$ or 5$^{th}$ administration of 2 mg of estradiol sulphamate the relationship between the maxima and minima is adjusted and **is comparable with medicament administered in 24 hour intervals**. The applicant is constructively arguing that after the 4$^{th}$ or 5$^{th}$ administration, intermittent administration yields the same result as continuous administration. By applicant's own analysis, daily administration would replenish the estradiol sulphamate supply and assure the presence of this drug in the plasma continuously and after the 4$^{th}$ dose, intermittent application would yield the same release profile. Therefore no distinction between the continuous application and 4$^{th}$ or 5$^{th}$ and subsequent intermittent administrations has been shown. Further note that the specification

provides 6 examples of one-time administration of estradiol sulphamate. No example of intermittent estraodiol sulphamate administration is given. Furthermore, the only exemplified dosage is 2 mg of estradiol sulphamate.

Applicants aver unexpected benefits residing in the claimed subject matter, yet fails to set forth evidence substantiating this belief as shown herein above. Evidence as to unexpected benefits must be " clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). The data provided by Applicants is not reasonably commensurate in scope with the instant claims. Absent claims commensurate with the showing of unexpected benefits, or a showing reasonably commensurate with the instant claims, such claims remain properly rejected under 35 USC 103.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Mojdeh Bahar

Mojdeh Bahar, J.D.
June 26, 2003

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